Notice of Allowability	Application No.	Applicant(s)	
	09/502,424	KILIAN ET AL.	
	Examin r	Art Unit	
	Malgorzata A. Walicka	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *Oct. 6 and Dec. 12, 2003*.
2. ☒ The allowed claim(s) is/are *1, 4-6,11-15, 27-29, 31, 61, 67,73-75, 93 and 108-118*.
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.
5. ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
   (a) ☐ The translation of the foreign language provisional application has been received.
6. ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
8. ☒ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No. ____.
   (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.
   (c) ☒ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the margin according to 37 CFR 1.121(d).

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1☐ Notice of References Cited (PTO-892)
2☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No. _____
4☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5☐ Notice of Informal Patent Application (PTO-152)
6☐ Interview Summary (PTO-413), Paper No._____ .
7☒ Examiner's Amendment/Comment
8☒ Examiner's Statement of Reasons for Allowance
9☐ Other .

The Supplementary Amendment and Petition for Extension of Time filed on Dec. 12, 2003 are acknowledged. Amendment to the Sequence Listing has been entered. Claims 1, 4-31, 33, 35-64, 67-70, 73-75, 86-91, 93-100, 102-118 as filed in the Amendment of October 6, 2003 are entered and are the subject of this Office Action.

Detailed Office Action

1. Objections

1. Drawings

The titles of Fig. 11A and 11L are not correct; they should be changed to: "Truncated telomerase".

1.1. Sequence listing

Objection to the sequence listing made in the Advisory Office Action is withdrawn because the amendment to the paper copy of the sequence listing have been filed.

2. Rejection withdrawal

The rejections of Claims 1, 11-15, 67, and 73-75 under 112, 1st paragraph are withdrawn in view of the amendments to the claims. As amended these claims (and new claim 110) are now limited to nucleic acids produced by the alternative splicing of the human telomerase genomic sequence at the specific

splice junctions defined in the specification. Therefore, the splice variant sequences disclosed in the specification are representative of the structures and functions of the genus now claimed.

The rejections of Claims 4, 11-15 and 73-75 under 112, 1st paragraph are withdrawn in view of the amendments to the claims. As amended these claims (and new claim 108) are now limited to nucleic acids encoding specific proteins/peptides for which the structures and functions are disclosed in the specification. It is noted the term "nucleic acid encodes" is taken to include 1.) nucleotide sequences in which the entire nucleic acid consists of an open reading frame for the recited protein/peptide without any additional 5' or 3' nucleotides and 2.) nucleotide sequences which comprise an AUG start codon followed by the open reading frame for the recited protein/peptide followed by a stop codon but does not include nucleic acids which comprise the open reading frame for the recited protein/peptide not immediately preceded by a start codon and immediately followed by a stop codon (i.e., the open reading frame for the recited protein/peptide embedded within a larger open reading frame) as such nucleic acids do not encode the recited protein/peptide but instead a larger protein/peptide which comprises the recited protein/peptide.

The rejections of Claims 5, 11-15 and 73-75 under 112, 1st paragraph are withdrawn in view of the amendments to the claims. As amended these claims are now limited to a genus of nucleic acids which share structural features (all will hybridize to the recited nucleic acids) and functional features (binding to telomerase RNA or telomerase activity) with the specific nucleic acids disclosed

in the specification. As such the specific species disclosed in the specification are representative of the claimed genus.

The rejections of Claims 6, 11-15, 27, 61 and 73-75 under 112, 1st paragraph are withdrawn in view of the amendments to the claims. As amended these claims (and new claims 109 and 111-113) are now limited to the specific nucleic acids disclosed in the specification or fragments thereof which all clearly have use as probes for the specific nucleic acids disclosed in the specification. As such the dislosed species of the specification are representative of the structures and functions of the claimed genus of nucleic acids.

3. Examiner's amendement

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Amendments to the specification:

a) Please replace the paragraph on page 1, lines 4-7 with the following amended paragraph:

This application is a continuation of United States Patent Application No. 09/108,401, filed June 30, 1998, now abandoned; which application claims the benefit of United States Provisional Application Nos. 60/051,410, filed July 1, 1997; 60/053,018, filed

July 19, 1997; 60/053,329, filed July 21, 1997; 60/054,642, filed August 4, 1997; and 60/058,287, filed September 9, 1997, all of which are incorporated by reference in their entirety.

b) Please replace the paragraph on page 4, lines 7-15 with the following amended paragraph:

In a related aspect, the invention provides a pair of oligonucleotide primers capable of specifically amplifying all or a portion of a nucleic acid molecule encoding human telomerase. In specific embodiments, the nucleic acid molecule comprises the sequence presented in Figure 1, Figure 11, or complements thereof. In preferred embodiments, the pair of primers is capable of specifically amplifying sequence comprising all or a part of alternative intron/exon 1, alternative intron/exon α, alternative intron/exon β, alternative intron/exon 2, alternative intron/exon 3, alternative intron/exon X or alternative intron/exon Y. In a related aspect, the invention provides an oligonucleotide that hybridizes specifically to a nucleic acid sequence in alternative intron/exon 1, alternative intron/exon α, alternative intron/exon β, alternative intron/exon 2, alternative intron/exon 3, alternative intron/exon X or alternative intron/exon Y.

c) At page 4, lines 28-29 replace --region 1, region α, region β, region 2, region 3 region X or region Y-- with --alternative intron/exon 1, alternative intron/exon α, alternative intron/exon β, alternative intron/exon 2, alternative intron/exon 3, alternative intron/exon X or alternative intron/exon Y--.

d) At page 6, line 3, replace --29-1132); SEQ ID NO: 5 sequences -- with --29-1132; SEQ ID NO: 5) sequences--.

e) At page 6, line 21, delete --that span an intron in the hT1 gene,--.

f) At page 7, line 24, replace --sequence α-- with —alternative intron/exon α--.

g) At page 7, line 26, insert --(SEQ ID NOS:18-33)-- following --telomerase--.

h) At page 7, line 28, insert --(SEQ ID NOS:2, 34-86 and 155)-- following --telomerase proteins--.

i) At page 8, line 2, insert --(SEQ ID NO:87)-- following --plasmid--.

j) At page 8, line 4, insert --(SEQ ID NO:88)-- following --plasmid--.

k) At page 8, line 6, insert --(SEQ ID NO:89)-- following --plasmid--.

l) At page 17, line 8, replace --the putative intronic sequences-- with --the putative alternative intron/exon sequences--.

m) At page 17 line 21, replace –nnucleotides--with--nucleotides--.

n) At page 18, line 10 delete "An amplified".

o) At page 19, line 22, insert --Because these regions are alternatively spliced in or out in the splice variants disclosed herein they are referred to as alternative intron/exon 1, 2, 3, α, β, X, and Y.-- following --variant proteins.--.

p) Please replace the paragraph on page 19, line 20 - page 20, line 2 with the following amended paragraph:

At least seven different putative alternative intron/exons appear to be retained in mRNAs (see Figure 7, which displays 6 of the 7 alternative intron/exons). The alternative intron/exons may be independently retained, thus, a particular mRNA may have none, any one, two, etc. up to seven alternative intron/exons. The maximum number of different mRNAs resulting from seven independently 7 spliced alternative intron/exons is 2^7, or 128 different mRNAs. DNA sequences of these alternative intron/exons are presented in Figure 10. The 5' most alternative intron/exon, called alternative intron/exon X, is an unknown length, and only a partial sequence is presented.

r) Please replace the paragraph on page 20, lines 3-9 with the following amended paragraph:

The reference telomerase sequence (Figure 1) includes alternative intron/exon α, and alternative intron/exon β. In the following discussion, the effect of presence/absence and location of each alternative intron/exon is presented on the basis that it is the only alteration. It will be appreciated that a particular alternative intron/exon may alter the sequence of the translated product, regardless of whether other alternative intron/exons are spliced in

or out. For example, the presence of alternative intron/exon 1 results in a frameshift and truncated protein, regardless of whether alternative intron/exons α, β, 2 or 3 are spliced in or out.

s) Please replace the paragraph on page 20, lines 10-15 with the following amended paragraph:

The presence of alternative intron/exon X results in a truncated protein that contains approximately 600 N-terminal amino acids and lacks all of the RTase motifs. The presence of alternative intron/exon Y at base 222 results in a frameshifted protein that terminates within three codons past the alternative intron/exon. As the Y intron/exon is very GC rich, approximately 78%, which is difficult to sequence, it is possible that alternative intron/exon Y causes an insertion of about 35 amino acids and not a frameshift.

t) Please replace the paragraph on page 20, lines 16-18 with the following amended paragraph:

Alternative intron/exon 1 at nucleotide 1950 is 38 bp and its presence in mRNA causes a frameshift and ultimate translation of a truncated protein (stop codon at nt 1973). This truncated protein contains only RTase domains 1 and 2.

u) Please replace the paragraph on page 20, lines 19-24 with the following amended paragraph:

Intron α, located at bases 2131-2166 is frequently observed spliced out of telomerase mRNA. A protein translated from such an RNA is deleted for 12 amino acids, removing RTase motif A. This motif appears to be critical for RT function; a single amino acid mutation within this domain in the yeast EST2 protein results in a protein that functions as a dominant negative and results in cellular senescence and telomere shortening.

v) At page 20, line 25, replace --the β-exon-- with --the alternative intron/exon β--.

w) At page 21, line 6, replace --Intron 2-- with --Alternative intron/exon 2--.

x) At page 21, line 9, replace --When intron 3 is retained, a smaller protein is also produced because the intron contains-- with --When alternative intron/exon 3 is retained, a smaller protein is also produced because the alternative intron/exon contains--

y) At page 21, lines 17, 18, and 25 replace --intron 3-- with --alternative intron/exon 3--.

z) Please replace the paragraph on page 22, lines 3-10 with the following amended paragraph:

The following table summarizes the splice variants and resulting proteins. For simplicity, only a single variant is listed for each resulting protein. Furthermore, as noted above, the presence of alternative intron/exon Y appears to cause a frameshift resulting in a truncated protein, but may cause an insertion. Thus, each reading frame of alternative intron/exon Y is presented and the table is constructed as if the insertion does not cause a truncated protein. An independent assortment of these known alternative intron/exons would lead to 128 different mRNA sequences. The DNA and amino acid sequences for the variants in Table 1 are presented in Figure 11.

aa) At page 26, line 26 replace --intron-- with --alternative intron/exon--.

ba) Please replace the paragraph on page 30, lines 5-19 with the following amended paragraph:

As discussed above, in preferred embodiments, expression of the various RNA species is monitored. The different species may be assayed by any method which distinguishes one of the species over the others. Thus, length determination by Northern, RNase probe protection, cloning and amplification are some of the available methods. In preferred embodiments, RNase probe protection and amplification are used. For RNase probe protection, the probe will generally be a fragment derived from the junction of the reference sequence and the alternative intron/exon sequence or derived from the sequence surrounding the alternative intron/exon insertion site. For example, a fragment of the reference telomerase that spans nucleotide 1950-1951 (e.g., nucleotides 1910-1980) will protect the reference sequence as a 71 base fragment, but will protect a telomerase with alternative intron/exon 1 as two fragments of 41 and 30 bases. In contrast, a fragment that contains nucleotides 1910-1950 and 30 bases of alternative intron/exon 1 will protect an alternative intron/exon 1 variant as a 71 base fragment and the reference telomerase as a 41 base fragment. Fragments for RNase probe protection are chosen usually in the range of 30 to 400 bases and are positioned to yield readily distinguishable protection products.

ca) At page 36, line 9 insert --(SEQ ID NO: 95) following — $N_3XN^*GUC(N_{>6})$--.

da) At page 37, line 12, replace --intron-- with --alternative intron/exon--

ea) At page 39, line 28, replace --intron-- with --alternative intron/exon--.

fa) At page 40, line 7, replace --introns-- with --alternative intron/exons--.

ga) At page 41, line 1, replace --introns-- with --alternative intron/exons--.

ha) At page 41, line 2, replace --intron-- with --alternative intron/exon--.

ia) At page 41, line 5, replace --intron-- with --alternative intron/exon--.

ja) At page 41, line 5, replace --introns-- with --alternative intron/exons--.

ka) At page 56, line 4, delete --or introns--.

la) At page 56, line 10, delete --intronic--.

ma) At page 62, lines 6-9, replace -- Three telomerase variants are constructed: pAKI.4 is telomerase with the beta region spliced out (Figure 13); pAKI.7 is telomerase with the alternative C-terminus insert 3 (Figure 14); and pAKI.14 is telomerase with the alpha region spliced out (Figure 15).-- with -- Three telomerase variants are constructed: pAKI.4 is telomerase with the alternative intron/exon beta spliced out (Figure 13); pAKI.7 is telomerase with the alternative C-terminus alternative intron/exon 3 (Figure 14); and pAKI.14 is telomerase with the alternative intron/exon alpha spliced out (Figure 15).--.

Amendments to the claims:

a) Cancel Claims 7-10, 16-26, 30, 33, 35-60, 62-64, 68-70, 86-91, 94-100, and 102-107

b) In Claim 1, line 2, replace --result in-- with --encode--.

In Claim 1, line 3, replace --encoding-- with --of--.

In Claim 1, line 5, replace --sequence X (comprising SEQ ID No:32) at-- with --alternative intron/exon X comprising SEQ ID No:32 at its 5'-end following--.

In Claim 1, lines 7-8, replace --sequence 1 (SEQ ID No:24) at-- with --alternative intron/exon 1 (SEQ ID No:24) following--.

In Claim 1, line 11, replace --sequence 2 comprising SEQ ID No:29 at-- with --alternative intron/exon 2 comprising SEQ ID No:29 at its 5'-end following--.

In Claim 1, lines 13-14, replace --sequence 3 (SEQ ID No:31) at-- with --alternative intron/exon 3 (SEQ ID No:31) following--.

In Claim 1, line 14, replace --SEQ ID No: 1.-- with --SEQ ID No: 1;--

c) In Claim 4, lines 1-2, replace --The nucleic acid molecule of Claim 1, wherein the nucleic acid molecule-- with --An isolated nucleic acid molecule which--.

In Claim 4, line 4, insert --or-- following --80-82,--.

d) In Claim 5, line 3, insert --or-- following --80-82,--.

e) In Claim 11, line 3, replace --109-- with --108--.

f) In Claim 27, line 2, delete --specifically--

In Claim 27, line 3, insert --under the following stringency conditions: 1 M Na^+, 5X SSPE, 0.5% SDS, 5X Denhardt's solution at 65° C-- following --according to claim 1--.

In Claim 27, line 7, delete --31--.

g) In Claim 61, line 2, replace --region 1-- with --alternative intron/exon 1--.

In Claim 61, lines 2-3, replace --region α-- with --alternative intron/exon α--.

In Claim 61, line 3, replace --region β-- with --alternative intron/exon β--.

In Claim 61, line 3, replace --region 2-- with --alternative intron/exon 2--.

In Claim 61, line 3, replace --region 3-- with --alternative intron/exon 3--.

h) In Claim 73, line 2, replace --109-- with --108--.

i) In Claim 74, line 2, replace --109-- with --108--.

j) In Claim 75, line 2, replace --109-- with --108--.

k) In Claim 108, line 1, insert --a peptide consisting of-- following --encoding--.

l) In Claim 110, lines 2-3, replace --sequence 3 (SEQ ID No:31) at-- with --alternative intron/exon 3 (SEQ ID No:31) following--.

m) In Claim 114, line 2, replace --region 1-- with --alternative intron/exon 1--.

In Claim 114, line 2, replace --region α-- with --alternative intron/exon α--.

In Claim 114, line 3, replace --region β-- with --alternative intron/exon β--.

In Claim 114, line 3, replace --region 2-- with --alternative intron/exon 2--.

In Claim 114, line 3, replace --region 3-- with --alternative intron/exon 3--.

In Claim 114, line 3, replace --region X-- with --and alternative intron/exon X--.

n) In Claim 115, line 7, replace --region 1-- with --alternative intron/exon 1--.

In Claim 115, line 8, replace --region β-- with --alternative intron/exon β--.

In Claim 115, line 9, replace --region 2-- with --alternative intron/exon 2--.

In Claim 115, line 10, replace --region 3-- with --alternative intron/exon 3--.

In Claim 115, line 10, replace --region X-- with --alternative intron/exon X--.

aa) In Claim 116, line 7, replace --region 1-- with --alternative intron/exon 1--.

In Claim 116, line 8, replace --region α-- with --alternative intron/exon α--.

In Claim 116, line 9, replace --region β-- with --alternative intron/exon β--.

In Claim 116, line 10, replace --region 2-- with --alternative intron/exon 2--.

In Claim 116, line 11, replace --region 3-- with --alternative intron/exon 3--.

In Claim 116, line 12, replace --region X-- with --alternative intron/exon X--.

In Claim 116, line 13, replace --region Y-- with --alternative intron/exon Y--.

Authorization for this examiner's amendment was given in an e-mail correspondence with Applicants' representative Carol Nottenburg on Dec. 23, 2003.

4. Allowance

Claims 1, 4-6, 11-15, 27-29, 31, 61, 67, 73-75, 93, 108-118 are allowed. The following is the examiner's reason for allowance.

Applicants disclose DNA molecules, encoding novel splice variants of human telomerase of SEQ ID NOs: 35, 37, 39, 42, 44, 46, 48, 50, 52- 54, 56-58, 60-62, 64-66, 68-70, 72-74, 76-78, 80-82, and 84-86. Said novel splice variants result from splicing in/out of the novel alternative intronic/exonic sequences having polynucleotide sequences of SEQ ID Nos: 23, 25, 27, 29, 30, 32, and 33. Applicants also disclose expression vectors and host cells expressing splice variants. In addition, applicants disclose DNA probes consisting of SEQ ID Nos: 23, 25, 27, 29, 30, 32, and 33 or their fragments. Furthermore, Applicants teach the primers for amplification of splice junction of alternative introns/exons of SEQ ID NOs: 23, 25, 27, 29, 30, 32, and 33. Applicants also disclose a method of determining a pattern of telomerase RNA expressing, wherein the probes originate from alternative introns/exons of SEQ ID NOs: 23, 25, 27, 29, 30, 32, and 33.

The claimed invention is novel and not obvious over the prior art, which is the US Patent No. 6,093, 809, effecting filing date May 6, 1997, issued to Cech et al. The patent discloses one splice variant of human telomerase reverse

transcriptase (SEQ ID NO: 225, encoded by SEQ ID NO: 224), which is identical to SEQ ID NO: 2 of the instant application and used by Applicant as a reference amino acid sequence. The patent does not suggest the alternative intronic-exonic sequences disclosed for the first time by Applicants.

While the Cech et al. patent clearly discloses or suggests many fragments of the telomerase gene disclosed and the use thereof as probes and amplification primers for this genes and fragments thereof, the patent does not suggest the specific probes, primers and methods of use thereof claimed in Claims 27-31, 61, 93, 109, and 111-118. Claims 27-31 and 109 recite the specific fragments of SEQ ID NOS: 23, 25, 27, 29, 30, 32, and 33 or their complements or fragments of SEQ ID NOS: 23, 29, 30 and 32. Claim 61 recites the specific nucleic acids sequences of SEQ ID NOS: 23, 25, 27, 29, and 30. Claims 111-113 recite fragments of SEQ ID NOS: 23, 29, 30, 32 and 33 or their complements. SEQ ID NOS: 23, 29, 30, 32 and 33 are not encompassed within the gene disclosed by Cech et al. While SEQ ID NOS: 25 and 27 are encompassed within the telomerase gene disclosed by Cech et al., there is nothing in the Cech et al. patent to suggest these alternative exon/intron fragments specifically. The disclosure of a large genus (in this case fragments of telomerase gene of SEQ ID NO: 224 disclosed by Cech et al.) does not make obvious a specific member thereof (i.e., SEQ ID NOS: 25 or 27 in the instant application) without some teaching leading to that specific member. Nothing in Cech et al. patent or the art as a whole would lead the skilled artisan to the specific alternative exon/intron of SEQ ID NOS: 25 or 27.

Claim 93 recites a pair of oligonucleotide primers in which one primer flanks nucleotide 1950, 2131-2166, 2287-2468, 2843, or 3157 of SEQ ID NO: 1 and the other primer comprises a fragment of SEQ ID NOS: 23, 25, 27, 29, 30, 32, and 33. While SEQ ID NOS: 25 and 27 are encompassed within the telomerase gene disclosed by Cech et al. as are some of the splice junctions recited in the claim, neither Cech et al. nor the prior art provides a reason to select a pair of amplification primers as claimed. In order to select such a pair the skilled artisan would need a reason to make a fragment of the Cech et al. telomerase gene with each of the claimed primers at opposite ends. While the Cech et al. patent and the prior art do suggest some specific fragments (for example the catalytic domain of the telomerase, or regions A, B, C and D within the catalytic domain), none of these would be produced by amplification with a primer pair as claimed.

Claim 114 recites a pair of oligonucleotide primers in which both primers comprise at least 15 nucleotides of SEQ ID NOS: 18, 23, 25, 27, 29, 30, or 32. While SEQ ID NOS: 25 and 27 are encompassed within the telomerase gene disclosed by Cech, neither Cech et al. nor the prior art provides a reason to select a pair of amplification primers as claimed, because neither Cech et al. nor the prior art suggest that they are alternative exonic/intronic fragments. In order to select such a pair the skilled artisan would need a reason to make a fragment of the Cech et al. telomerase gene with each of the claimed primers at opposite ends. While the Cech et al. patent and the prior art do suggest some specific fragments (for example the catalytic domain of the telomerase, or regions A, B, C

and D within the catalytic domain), none of these would be produced by amplification with a primer pair as claimed.

Claims 115, 117 and 118 recite hybridization methods which utilize fragments of SEQ ID NOS: 23, 27, 29, 30, or 32 as probes. SEQ ID NOS: 23, 29, 30, and 32 are not encompassed within the gene disclosed by Cech et al. While SEQ ID NO:27 is encompassed within the telomerase gene disclosed by Cech, there is nothing in the Cech et al.'s patent to suggest selecting a hybridization probe from this region specifically. While the Cech et al. patent and the prior art do suggest some specific regions of the telomerase gene of particular interest such that the skilled artisan would wish to have a probe to that fragment of the gene (for example the catalytic domain of the telomerase, or regions A, B, C and D within the catalytic domain), none of these would suggest a probe from the region of SEQ ID NO: 27.

Claims 116-118 recite hybridization methods which utilize 2 or more probes which are fragments of SEQ ID NOS: 18, 23, 25, 27, 29, 30, or 32. While Cech et al. do suggest hybridization methods using probes which are fragments of the disclosed telomerase gene, neither Cech et al. nor the prior art suggest a reason to use two or more probes in the same assay that are fragments of these specific alternative exonic/intronic sequences.

The invention claimed by Applicants has clinical application in diagnosis and treatment of many diseases related to cancer and aging.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

Art Unit 1652

Patent Examiner